

REMARKS

The Official Action of November 17, 2005, has been carefully studied. The claims in the application remain as claims 2-6, 8-15 and 25-30 (plus new dependent claim 31), none of which have been rejected on the basis of prior art, whereby applicants understand that claims 2-6, 8-15 and 25-30 are deemed by the PTO to define novel and unobvious subject matter. Applicants submit that all of applicants' claims define patentable subject matter and therefore should be allowed, whereby applicants respectfully request favorable reconsideration and allowance.

A review of the English translation of the above-identified application, originally filed in Japanese, has revealed an important translational error at page 9, line 6, which error has been corrected above. In more detail, the Z value in the English translation is incorrectly defined by the formula (measuring value - average for the patients **with** bone metastasis)/(standard deviation of a patient without one metastasis). In this translation, "**with** bone metastasis" (lines 6-7) is a translational error. The Japanese text is shown on the attached sheet corresponding to page 6, line 23 of PCT/JP99/04480. Thus, the Japanese text should have been

translated "without bone metastasis", not "with bone metastasis".

As the Japanese text is the original disclosure, there is no question of any new matter. It will also be noted that the same Japanese text appears on the 24<sup>th</sup> line of the same page. The second presentation of this text was translated correctly at page 9, line 7 of the English translation (last word).

The same translational error was carried over to and has been found in claims 6 and 30, and has thus been corrected in claims 6 and 30 above.

Claims 2-6, 8-15 and 25-30 have been rejected under the second paragraph of Section 112. The rejection is respectfully traversed for the reasons set forth below, wherein the paragraph designations in lowercase letters correspond to those of paragraph 7 of the Office Action.

(a) There seems to be two objections stated against claim 6. First, the rejection asserts that while the preamble of claim 6 reads on using two markers, the claim recites testing of blood for only one marker. While applicants respectfully disagree, claim 6 has nevertheless been amended to place it in better form for U.S. practice by reciting the following:

"the improvement wherein said testing comprises measuring for both osteocalcin and one marker selected from the group consisting of BALP, PICP and PINP, as well as measuring for ICTP,

determining a Z value for each of said osteocalcin and said marker, each said Z value being determined by dividing the difference between said measured value for said patient and an average value for patients without bone metastasis, by a standard deviation of a patient without bone metastasis, and determining a crossover index by dividing said Z value for osteocalcin by said Z value for BALP, PICP to PINP, and

determining ICPT level,

said crossover index and said ICPT level providing a diagnosis of progression of bone metastasis in the treatment of said patient for said cancer."

By such amendments, there should now be no doubt that claim 6 is intended to, and does indeed, recite the use of two markers.

The rejection also asserts that the steps are incongruent with the preamble and moreover do not provide information as to how amelioration and/or exacerbation of metastasis is assessed. Applicants most strenuously disagree and traverse the conclusion so stated by the PTO.

A main characteristic feature of the present invention resides in the use of two markers: one is a marker

that reflects the activity of osteoblasts and the other is a marker that reflects the activity of osteoclasts; or the use of a marker that reflects the activity of osteoblasts. Once the claimed process has been carried out, it is then that one skilled in the art such as a medical doctor assesses amelioration and/or exacerbation of metastasis based on professional knowledge. Therefore, applicants respectfully maintain that information as to how amelioration and/or exacerbation of metastasis is assessed is within the skill of the art and does not have to be recited in claim 6.

However, applicants have added a recitation "assessing or judging amelioration and/or exacerbation of metastasis in comparison with existing control data for CR, PD, IMP and NC", and this should further obviate the rejection.

(b) Applicants do not understand what is unclear about the criticized recitation appearing in claims 6, 8 and 30, and particularly does not understand the language "such as a particular number means for example drugs are effective or bone metastasis has progressed." Is the rejection stating that the claims should recite particular means, such as particular drugs, for treating bone metastasis? Applicants strongly traverse any such contention.

Again, a main characteristic feature of the present invention resides in the use of two markers: one is a marker that reflects the activity of osteoblasts and the other is a marker that reflects the activity of osteoclasts; or the use of a marker of a marker that reflects the activity of osteoblasts. How the bone metastasis is treated is not an element of the present invention, as any such treatment can be used (after diagnosis according to the present invention) now known or in the future discovered.

If by "a particular number" means that the PTO believes that the rejected claims should contain any such particular number (number of what? markers?), applicants respectfully disagree. The addition to the claims of any particular number would make the claims unduly restricted. Applicants' claims are clear to those skilled in the present art, individuals who are highly skilled. Applicants' claims define novel and unobvious subject matter as now acknowledged by the absence of any prior art rejections, and meet all the requirements of the first paragraph of Section 112.

In short, the claims define what the applicants regard as their invention, and there is no question that such claims would be fully understandable by those skilled in the art, again it being understood that those skilled in the art are highly skilled individuals.

(c) Applicants have complied with the Examiner's suggestion to use classical Markush language, even though such classical markoush language is not required noting MPEP 2173.05(h).

(d) The rejection asserts that it is not clear from claims 8-17 how the two markers are used in ascertaining efficacy of a drug and that the method steps are not clear. Again, with respect, this conclusion by the PTO makes no sense to applicants. The efficacy of any particular drug has nothing to do with applicants' invention which relates to **diagnosis**. Respectfully, the rejection is unreasonable.

Applicants have nevertheless added a feature like the feature added to claim 6 and discussing above in part (a) which should further obviate the rejection.

The rejection also asserts that it is not clear how the Z values obtained from the markers relate to the efficacy of the drug used in cancer treatment, and that it is not noted in the claims that a particular number obtained from the Z values means the drugs are effective or not. As stated above, a main characteristic feature of the present invention resides in the use of two markers: one is a marker that reflects the activity of osteoblasts and the other is a marker that reflects the activity of osteoclasts; or the use of a marker that reflects the activity of osteoblasts. If such

information as a particular number from the Z values is recited in these claims, it would make each of the claims unduly restrictive.

The rejection further asserts that neither claim 6 (not included in the (d) part of this rejection) nor its dependent claims establish what a Z value means in regard to diagnosing amelioration and/or exacerbation. However, it should be noted that claim 6 recites not only "Z value" but also "crossover index" and that the value of a crossover index can be an indicator for diagnosis or amelioration and/or exacerbation. In this case, if a particular number from the crossover indexes is recited in the claims, it would make each of the claims unduly restrictive.

(e) Applicants respectfully repeat by reference the same remarks made above in part (a) with respect to claim 6.

(f) Claim 8 has been appropriately corrected.

(g) Applicants' remarks as made above with respect to claim 6 are respectfully repeated by reference, claim 30 having been amended in a similar way in the paragraph now using the classical Markush language. Also, claim 31 has been added, this claim being patentable because it depends from and includes claim 30.

Applicants believe the claims as previously drafted, particularly considered in light of applicants' specification (fully consistent with the law), would not have been confusing to those skilled in the art, and therefore the claims in their previous form are fully in accordance with the second paragraph of Section 112. At **worst**, the claims in their previous forms might be considered objectionable, but **only** as to form, requiring no substantial amendments relating to patentability.

Nevertheless, in deference to the Examiner's views and to attempt to minimize argumentation, a number of cosmetic amendments have been made above. These amendments are submitted to be of a formal nature only, i.e. made to place the claims in improved form for U.S. practice or the Examiner's understanding of what is necessary or desirable for U.S. practice. Applicants believe and submit that at least for the most part such amendments are not "narrowing" amendments because the scope of the claims has not been reduced in these regards. No limitations have been added in these regards and none are intended.

Withdrawal of the rejection is in order and is respectfully requested.

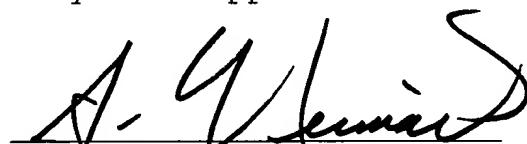
Appl. No. 09/763,370  
Amd. dated May 17, 2006  
Reply to Office Action of November 17, 2005

Applicants believe that all issues raised in the Office Action have been addressed above in a manner favorable to allowance of the present application. Accordingly, applicants respectfully request favorable reconsideration and early formal allowance.

Respectfully submitted,

BROWDY AND NEIMARK, P.L.L.C.  
Attorneys for Applicant

By



Sheridan Neimark  
Sheridan Neimark  
Registration No. 20,520

SN:kg  
Telephone No.: (202) 628-5197  
Facsimile No.: (202) 737-3528  
G:\BN\Y\YUAS\OGATA4\PTO\PCTAMD 17MAY06.doc